

Section I. (The Claims)

1. (Previously Presented) A method for obtaining a singular cell model capable of reproducing *in vitro* a metabolic idiosyncrasy of humans, wherein said model comprises a set of recombinant adenoviral expression vectors that confer to transformed cells a phenotypic profile of drug biotransformation enzymes designed at will, in order to reproduce the metabolic idiosyncrasy of humans, said method comprising:

- a) Transforming human cells of hepatic origin expressing reductase activity with a set of more than one recombinant adenoviral expression vectors comprising an ectopic DNA sequence that codes for drug biotransformation enzymes selected from among Phase I drug biotransformation enzyme and Phase II drug biotransformation enzyme,

wherein each expression vector comprises an ectopic DNA sequence that codes for a different Phase I or Phase II drug biotransformation enzyme, selected from the group consisting of:

- (i) a DNA sequence transcribed in the sense mRNA of a Phase I or a Phase II drug biotransformation enzyme ("sense vector"); and
- (ii) a DNA sequence transcribed in the anti-sense mRNA of a Phase I or a Phase II drug biotransformation enzyme ("anti-sense vector");

wherein the expression of said ectopic DNA sequences in the cells transformed with one or more of the aforementioned expression vectors confers on the transformed cells specific phenotypic profiles of Phase I or Phase II drug biotransformation enzymes,

to obtain expression vector cells that transitorily express said ectopic DNA sequences and present a different phenotypic profile of Phase I or Phase II drug biotransformation enzymes, and

- b) building a singular cell model capable of reproducing *in vitro* the metabolic idiosyncrasy of humans from said cells transformed with the expression vectors so that the result is the expression of any phenotypic profile of Phase I or Phase II drug biotransformation enzymes desired.

2. (Previously Presented) Method according to claim 1, wherein said Phase I and Phase II drug biotransformation enzymes are selected from the group consisting of oxygenases, oxydases, hydrolases and conjugation enzymes.

3. (Previously Presented) Method according to claim 1, wherein said Phase I and Phase II drug biotransformation enzymes are selected from the group consisting of monooxygenases dependent on CYP450, flavin-monooxygenases, sulfo-transferases, UDP-glucuronyl transferase, epoxide hydrolase and glutathione transferase.

4. (Previously Presented) Method according to claim 1, wherein said ectopic DNA sequence coding for a Phase I or Phase II drug biotransformation enzyme is selected from the group consisting of: DNA sequences transcribed in the sense mRNA of CYP450 isoenzymes; anti-sense mRNA of CYP450 isoenzymes; DNA sequences transcribed in the sense mRNA of oxygenases, oxidases, hydrolases and conjugation enzymes involved in drug biotransformation; and DNA sequences transcribed in the anti-sense mRNA of oxygenases, oxidases, hydrolases and conjugation enzymes involved in drug biotransformation.

5. (Previously Presented) Method according to claim 1, wherein said ectopic DNA sequence coding for a Phase I or Phase II drug biotransformation enzyme is selected from the group consisting of: DNA sequences transcribed in the sense mRNA of CYP 1A1, CYP 1A2, CYP 2A6, CYP 2B6, CYP 2C8, CYP 2C9, CYP 2C18, CYP 2C19, CYP 2D6, CYP 2E1, CYP 3A4, CYP 3A5, GST(A1); DNA sequences transcribed in the anti-sense mRNA of CYP 1A1, CYP 1A2, CYP 2A6, CYP 2B6, CYP 2C8, CYP 2C9, CYP 2C18, CYP 2C19, CYP 2D6, CYP 2E1, CYP 3A4, CYP 3A5, GST(A1); DNA sequences transcribed in the sense mRNA of flavin-monooxygenases, sulfo-transferases, UDP-glucuronyl transferase, epoxide hydrolase and glutathione transferase; and DNA sequences transcribed in the anti-sense mRNA of flavin-monooxygenases, sulfo-transferases, UDP-glucuronyl transferase, epoxide hydrolase and glutathione transferase.

6. (Original) Method according to claim 1, wherein said ectopic DNA sequence coding for a Phase I or Phase II drug biotransformation enzyme is a DNA sequence transcribed in the sense mRNA of a Phase I or Phase II drug biotransformation enzyme.

7. (Original) Method according to claim 1, wherein said ectopic DNA sequence coding for a Phase I or Phase II drug biotransformation enzyme is a DNA sequence transcribed in the anti-sense mRNA of a Phase I or Phase II drug biotransformation enzyme.

8. (Original) Method according to claim 1, which comprises the combined use of variable amounts of said expression vectors comprising ectopic DNA sequences coding for the drug biotransformation enzymes selected from among Phase I drug biotransformation enzymes and Phase II drug biotransformation enzymes.

9. (Currently amended) A human cell model obtainable by a method according to claim 1 capable of reproducing *in vitro* the metabolic idiosyncrasy of humans characterized in that said cells are human cells of hepatic origin expressing reductase activity, wherein said cells are transformed with a set of more than one recombinant adenoviral expression vectors, wherein each expression vector comprises an ectopic DNA sequence that codes for a different Phase I or Phase II drug biotransformation enzyme, selected from among:

(i) a DNA sequence transcribed in the sense mRNA of a Phase I or Phase II drug biotransformation enzyme ("sense vector"); and

(ii) a DNA sequence transcribed in the anti-sense mRNA of a Phase I or Phase II drug biotransformation enzyme ("anti-sense vector");

wherein the transitory expression of said ectopic DNA sequences in the cells transformed with one or more of the aforementioned expression vectors confers the transformed cells specific phenotypic profiles of Phase I or Phase II drug biotransformation enzymes.

10. (Cancelled)

11. (Previously Presented) A method for studying the metabolism, pharmacokinetics, potential idiosyncratic hepatotoxicity, and/or potential medicament interactions of a drug, said method comprising placing said drug in contact with a singular cell model capable of reproducing *in vitro* the metabolic idiosyncrasy of humans obtained according to the method of claim 1.

12. (Cancelled)

13. (Previously Presented) A method to confer to any cell line the capacity to metabolize xenobiotics in a controllable manner by means of a set of more than one adenoviral expression vectors selected from the group consisting of Phase I enzymes, Phase II enzymes, and cytochrome P450 reductase, said method comprising the transfection of said cell line with said adenoviral expression vectors in order to confer to the transformed cells a phenotypic profile designed to metabolize xenobiotics,

characterised in that the transformation of a cell line expressing cytochrome P450 reductase activity is carried out with a set of more than one expression vectors comprising ectopic DNA sequences coding P450 enzymes involved in the xenobiotic biotransformation, wherein each expression vector comprises an ectopic DNA sequence transcribing for the sense mRNA of a different CYP enzyme, and wherein the expression of said ectopic sequences in the transformed cells confers to them a transitory xenobiotic metabolic profile.

14. (New) Cells according to claim 9, wherein said Phase I and Phase II drug biotransformation enzymes are selected from among oxygenases, oxydases, hydrolases and conjugation enzymes.

15. (New) Cells according to claim 9, wherein said Phase I and Phase II drug biotransformation enzymes are selected from among monooxygenases dependent on CYP450, flavin-monoxygenases, sulfo-transferases, UDP-glucoronyl transferase, epoxide hydrolase and glutation transferase.

16. (New) Cells according to claim 9, wherein said ectopic DNA sequence coding for a Phase I or Phase II drug biotransformation enzyme is selected from among the group of DNA sequences transcribed in the sense mRNA or anti-sense mRNA of CYP450 isoenzymes and DNA sequences transcribed in the sense mRNA or anti-sense mRNA of oxygenases, oxidases, hydrolases and conjugation enzymes involved in drug biotransformation.

17. (New) Cells according to claim 9, wherein said ectopic DNA sequence coding for a Phase I or Phase II drug biotransformation enzyme is selected from among the group of DNA sequences transcribed in the sense mRNA or anti-sense mRNA of CYP 1A1, CYP 1A2, CYP 2A6, CYP 2B6, CYP 2C8, CYP 2C9, CYP 2C18, CYP 2C19, CYP 2D6, CYP 2E1, CYP 3A4, CYP 3A5, GST(A1), and DNA sequences transcribed in the sense mRNA or anti-sense mRNA of flavin-monoxygenases, sulfo-transferases, UDP-glucoronyl transferase, epoxide hydrolase or glutation transferase.

18. (New) Cells according to claim 9, wherein said ectopic DNA sequence coding for a Phase I or Phase II drug biotransformation enzyme is a DNA sequence transcribed in the sense mRNA of a Phase I or Phase II drug biotransformation enzyme.

19. (New) Cells according to claim 9, wherein said ectopic DNA sequence coding for a Phase I or Phase II drug biotransformation enzyme is a DNA sequence transcribed in the anti-sense mRNA of a Phase I or Phase II drug biotransformation enzyme.

20. (New) Cells according to claim 9, wherein the cells comprises variable amounts of said expression vectors comprising ectopic DNA sequences coding for the drug biotransformation enzymes selected from among Phase I drug biotransformation enzymes and Phase II drug biotransformation enzymes.